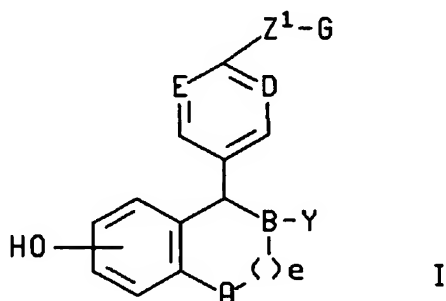


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Application No. 10/615,282

# AMENDMENTS TO THE CLAIMS

Claims 1.-22. (canceled)

23. (new) A method of inhibiting inflammatory bowel disease in a mammal, the method comprising administering to a mammal in need of inhibition of inflammatory bowel disease a therapeutically effective amount of a compound of formula I



wherein:

A is selected from CH<sub>2</sub> and NR;

B, D and E are independently selected from CH and N;

Y is

- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- (c) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, optionally substituted with 1-2 substituents independently selected from R<sup>4</sup>;
- (d) C<sub>3</sub>-C<sub>8</sub> cycloalkenyl, optionally substituted with 1-2 substituents independently selected from R<sup>4</sup>;
- (e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;
- (f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>- and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>; or

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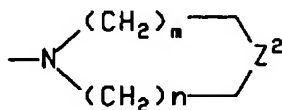
- (g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, -NR<sup>2</sup>-, and -S(O)<sub>n</sub>-, optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;

Z<sup>1</sup> is

- (a) -(CH<sub>2</sub>)<sub>p</sub>W(CH<sub>2</sub>)<sub>q</sub>-;  
(b) -O(CH<sub>2</sub>)<sub>p</sub>CR<sup>5</sup>R<sup>6</sup>-;  
(c) -O(CH<sub>2</sub>)<sub>p</sub>W(CH<sub>2</sub>)<sub>q</sub>-;  
(d) -OCHR<sup>2</sup>CHR<sup>3</sup>-; or  
(e) -SCHR<sup>2</sup>CHR<sup>3</sup>-;

G is

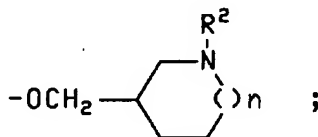
- (a) -NR<sup>7</sup>R<sup>8</sup>;  
(b)



wherein n is 0, 1 or 2; m is 1, 2 or 3; Z<sup>2</sup> is -NH-, -O-, -S-, or -CH<sub>2</sub>-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R<sup>4</sup>; or

- (c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R<sup>4</sup>;

Z<sup>1</sup> and G in combination may be



W is

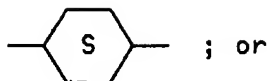
- (a) -CH<sub>2</sub>-;  
(b) -CH=CH-;  
(c) -O-;

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- (d)  $-\text{NR}^2-$ ;
- (e)  $-\text{S}(\text{O})_n-$ ;
- (f)



- (g)  $-\text{CR}^2(\text{OH})-$ ;
- (h)  $-\text{CONR}^2-$ ;
- (i)  $-\text{NR}^2\text{CO}-$ ;
- (j)



- (k)  $-\text{C}\equiv\text{C}-$ ;

R is hydrogen or  $\text{C}_1$ - $\text{C}_6$  alkyl;

$\text{R}^2$  and  $\text{R}^3$  are independently

- (a) hydrogen; or
- (b)  $\text{C}_1$ - $\text{C}_4$  alkyl;

$\text{R}^4$  is

- (a) hydrogen;
- (b) halogen;
- (c)  $\text{C}_1$ - $\text{C}_6$  alkyl;
- (d)  $\text{C}_1$ - $\text{C}_4$  alkoxy;
- (e)  $\text{C}_1$ - $\text{C}_4$  acyloxy;
- (f)  $\text{C}_1$ - $\text{C}_4$  alkylthio;
- (g)  $\text{C}_1$ - $\text{C}_4$  alkylsulfinyl;
- (h)  $\text{C}_1$ - $\text{C}_4$  alkylsulfonyl;
- (i) hydroxy ( $\text{C}_1$ - $\text{C}_4$ )alkyl;
- (j) aryl ( $\text{C}_1$ - $\text{C}_4$ )alkyl;
- (k)  $-\text{CO}_2\text{H}$ ;
- (l)  $-\text{CN}$ ;
- (m)  $-\text{CONHOR}$ ;
- (n)  $-\text{SO}_2\text{NHR}$ ;
- (o)  $-\text{NH}_2$ ;
- (p)  $\text{C}_1$ - $\text{C}_4$  alkylamino;
- (q)  $\text{C}_1$ - $\text{C}_4$  dialkylamino;

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- (r) -NHSO<sub>2</sub>R;
- (s) -NO<sub>2</sub>;
- (t) -aryl; or
- (u) -OH.

R<sup>5</sup> and R<sup>6</sup> are independently C<sub>1</sub>-C<sub>8</sub> alkyl or together form a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring;

R<sup>7</sup> and R<sup>8</sup> are independently

- (a) phenyl;
- (b) a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring, saturated or unsaturated;
- (c) a C<sub>3</sub>-C<sub>10</sub> heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
- (d) H;
- (e) C<sub>1</sub>-C<sub>8</sub> alkyl; or
- (f) form a 3 to 8 membered nitrogen containing ring with R<sup>6</sup> or R<sup>6</sup>;

R<sup>7</sup> and R<sup>8</sup> in either linear or ring form may optionally be substituted with up to three substituents independently selected from C<sub>1</sub>-C<sub>8</sub> alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by R<sup>7</sup> and R<sup>8</sup> may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

n is 0, 1 or 2;

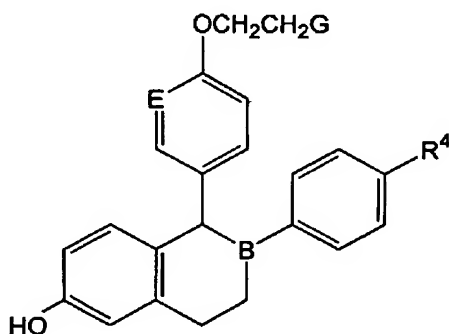
p is 0, 1, 2 or 3; and

q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt thereof.

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24. (new) A method of inhibiting inflammatory bowel disease in a mammal, the method comprising administering to a mammal in need of inhibition of inflammatory bowel disease a therapeutically effective amount of a compound of the formula



wherein G is



25. (new) A method of Claim 23 wherein the compound of formula I is selected from the group consisting of:

*Cis*-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol,

(-)-*Cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol,

*Cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol, and

*Cis*-6-(4'-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol, or a pharmaceutically acceptable salt of the compound.

26. (new) A method of inhibiting inflammatory bowel disease in a mammal, the method comprising administering to a mammal in need of inhibition of inflammatory bowel disease a therapeutically effective amount of (-)-*cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol or a pharmaceutically acceptable salt thereof.